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Early and late immunity results with scarlatinal streptococcus toxin.

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From the results noted with the Dick test[1] among large numbers of persons of different age and social groups, it was evident that a close analogy would be found not only in the natural antitoxic immunity but also in the artificially induced antitoxic immunity to scarlet fever as well as to diphtheria. The results with the Dick re-test on over 1,200 individuals (originally positive) injected in schools, institutions and private practice, justify the conclusion that an active immunity can not only be developed in most persons, but that it is persistent in 80-90 per cent of those successfully immunized. About 10 to 20 per cent of the injected may show a slightly positive Dick reaction after having had a negative reaction at a previous test. The antitoxic immunity in these persons can be quickly re-established with a few doses of toxin. My own three children, whose ages are two, three and one-half and five years, and who were injected 14 months ago with three doses of the toxin, still give a negative Dick retest.

Our standard solution of toxin for the Dick test is just twice as strong as that recommended by the Dicks. It indicates better the susceptible group of children by their more pronounced positive reactions. Slight positive reactors are not considered as being very susceptible to the toxic phase of scarlet fever. The stronger toxin dilution also indicates that the person injected with it and giving a negative Dick reaction at the retest is more certain to be immune to scarlet fever. It also shows in the naturally immune a larger amount of antitoxic antibodies and therefore these individuals are less likely to give positive reactions at subsequent tests. A method of standardization of the toxin for the Dick test was suggested by Zingher[2] in a previous communication.

The work now covers a period of fifteen months. We used small doses at first to avoid the severe local and constitutional

[1] Zingher, Abraham, *J. Am. Med. Assn.*, 1924, lxxxiii, 432.

[2] Zingher, Abraham, The Dick Test and Active Immunization with Scarlet Fever Streptococcus Toxin. *Am. J. Public Health*, March, 1924.

reactions described by the Dicks in their original communication on active immunization with the scarlatinal toxin. With increasing experiment we have gained more confidence in the use of the toxin, and have not hesitated to increase the dosage from the original three doses recommended, 100, 250, and 500 skin test doses, to four doses of 250, 1000, 2000 and 3000 or 4000, depending on the age and reactions of the injected person.

The study of the immunity response has been very interesting. Just as in the active immunization against diphtheria, we find in the immunization against scarlet fever also, that those who have a slight amount of antitoxin and show a ± reaction give a better and prompter response than those with a + or ++ reaction. But even most of the ++ reactors can be fully immunized with one or two series of toxin injections. Since using the larger doses of toxin, we have obtained with one series of injections about 70 per cent negative Dick re-tests, and about 26 per cent of slightly positive re-tests among persons who originally gave ++ or + reactions. We have not found that the addition of phenol as a preservative to the toxin interfered in the slightest degree with the immunizing value of the toxin.

In two private schools, the Ethical Culture School and the Horace Mann School, not a single case of scarlet fever developed among the injected children, although outbreaks of scarlet fever developed in both schools 3 to 9 months afterwards. At the Ethical Culture School about 200 out of 800 children, and at the Horace Mann School about 250 out of 900 children, have been injected.

It is interesting to note that the negative Dick reaction in "naturally" immune persons is quite permanent. Of 2,580 such negative reactors re-tested after 2 to 12 months, 2,545 of 98.6 per cent, continued to show a negative Dick reaction. This indicates that in the persistence of the natural immunity to scarlet fever we have a close similarity to that noted to diphtheria. With the Schick test we had seen on re-testing over 12,000 naturally immune school children after a period of 6 months to 3 years, that only 11 children (or less than 0.1 per cent) subsequently showed a positive Schick reaction.

CONCLUSION.

1. A complete antitoxic immunity to scarlet fever was produced by 4 doses of scarlet fever toxin (250, 1000, 2000 and 3000 skin test doses) in 70 per cent of injected persons, and a

partial immunity in 26 per cent. A second series of toxin injections successfully immunized most of the refractory cases.

2. Subsequent exposure to scarlet fever showed that the induced active immunity protected the children from infection.

3. From 10 to 20 per cent of individuals who gave a negative Dick reaction after toxin injections showed a slightly positive reaction at later re-tests.

4. Groups of children who were re-tested from 9 to 14 months after the toxin injections show by a negative Dick retest that the immunity can last for at least that period of time.

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Immunity results with diphtheria toxoid (modified toxin anatoxin) and 1/10 L + mixtures of toxin antitoxin.

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The 1/10 L+ mixture of diphtheria toxin-antitoxin, when prepared with a slight excess of free toxin so that 5 cc. will kill a guinea pig in 5 to 7 days, is an efficient immunizing agent. Three doses, each 1 cc., will immunize from 90 to 98 per cent of injected persons. The fact, however, that an underneutralized mixture has to be used which produces the local effects of free toxin at the site of injection; that the mixture has to be very carefully prepared so that the amount of free or partly bound toxin is not in excess; and finally that the mixture on standing loses some of its immunizing value, indicates that such a mixture is not yet the ideal preparation for the universal immunization of all children of school age and pre-school age. In diphtheria toxoid (anatoxin) we have such a preparation. It is easily made by adding 0.25 to 0.4 per cent formalin to the toxin, and leaving the formalinized toxin in the incubator for 30 days. The preparation is stable, *non-toxic* and highly efficient as an immunizing agent. With a preparation sent us by Ramon, we injected one-half of the children in three large schools, the other half being injected with 1/10 L+ toxin-antitoxin. The dose of the anatoxin